

# Intracranial Pressure Monitoring: Relationship between Indices of Cerebrovascular Reserve, System Bandwidth, and Cerebral Perfusion

M.L. Daley<sup>1</sup>, Sulhyung Han<sup>1</sup>, Shelly D. Timmons, M.D.<sup>2</sup>, M. Pourcyrus<sup>3</sup>, and C. W. Leffler<sup>4</sup>

<sup>1</sup>Department of Electrical and Computer Engineering, University of Memphis, Memphis, TN

<sup>2</sup>Department of Neurosurgery, University of Tennessee Health Science Center, Memphis, TN

<sup>3</sup>Depts. Pediatrics, Obstetrics/Gyn., and Physiology, University Tenn. Health Science Ctr., Memphis, TN

<sup>4</sup>Departments of Physiology and Pediatrics, University of Tennessee Health Sciences Ctr., Memphis, TN

**Abstract:** Loss of cerebrovascular reserve with the resultant increase of cerebral perfusion, and disruption of capillary fluid balance generally leads to the development of cerebral edema, a serious secondary complication of traumatic brain injury. Two indices of cerebrovascular reserve derived from recordings of intracranial pressure (ICP) and arterial blood pressure (ABP) have been proposed [1-3]. The purpose of this study was to examine the relationship between changes of arteriolar resistance, cerebral perfusion, system bandwidth, and the indices of cerebrovascular reserve during dilatory challenge induced by ventilation with CO<sub>2</sub>. Steady state values of arteriolar diameter significantly increased during hypercapnia resulting in a decrease of arteriolar resistance by more than 90%. Cerebral perfusion pressure (CPP) was found to range from -18% to 12%. Significant correlation between percent change of relative flow and either indices of cerebrovascular reserve, arteriolar resistance, or system bandwidth were not determined. System bandwidth between ABP and ICP and the Correlation Index of cerebrovascular reserve (CorrX), were found to be exponentially correlated with values ranging from 0.85 to .99 with a group (n=5) mean (+S.D.) of 0.94 (+0.06). Such a relationship suggests that near minimal tone, further losses of tone lead to changes of stiffness that produce large changes in system bandwidth.

**Key Words:** cerebral perfusion, cerebrovascular reserve, and system bandwidth

## I. INTRODUCTION

Approximately 2 million head injuries occur each year in the United States, producing a brain injury rate of 175 to 200 per 100,000 population and causing as many as 56,000 deaths per year [4]. The economic and emotional toll of this public health burden is very high [4]. A serious secondary complication following traumatic brain injury is cerebral edema. Disruption of capillary fluid balance between plasma and cerebrospinal fluid as the result of loss of cerebrovascular reserve and increased cerebral perfusion is a primary mechanism that leads to the development of cerebral edema.

Techniques to continuously monitor cerebrovascular reserve in the intensive care of the patient with severe head-injury have been proposed. Specifically, two numerical indices, the correlation index (CorrX) and the pressure reactivity index (PrX), derived from correlation of the dynamic features of the intracranial pressure (ICP) and arterial blood pressure (ABP) recordings have been defined [1-3]. The CorrX index is based on laboratory observations that during normal cerebral vascular tone the ICP and ABP recordings are not similar [1,2]. In contrast,

during deep hypercapnia and maximal vascular dilation and loss of cerebral vascular reserve, when the brain has lost the ability to regulate blood flow, these pressure signals are similar [1,2]. The PrX index is numerically derived from the correlation of the low frequency characteristics of the ICP and ABP recordings and designed to continuously monitor slow spontaneous waves in ICP and ABP [3]. This index is based on epidemiologic clinical observations that indicated that a sustained high value during the first 2 days following injury was indicative of an unfavorable outcome [3].

The purpose of this study was to examine the relationship between changes of arteriolar resistance, cerebral perfusion, system bandwidth and the proposed indices of cerebral vascular reserve.

## II. METHODS

Using an approved protocol from the institutional review boards involved and similar to those procedures previously described [2], 18  $\alpha$ -chloralose anesthetized 5 piglets ranging in weight from 2 to 4 kg were used in this study. In each piglet a cranial window was placed and video micrometer recordings were made as described previously [2]. A fluid-filled catheter inserted in either the brachial artery or femoral artery was used to record ABP, and ICP was recorded using fluid filled catheter linked coupled to a port of the cranial window.

Severe hypercapnia was used to maximally dilate the arterial vasculature. Specifically, the preparation was ventilated with 8.5% CO<sub>2</sub>. Each time this manipulation occurred, ICP increased and ABP decreased over a time course of approximately 5 to 8 minutes to a new steady-state condition. This state was characterized by an arterial carbon dioxide tension (PaCO<sub>2</sub>) above 70 mm Hg.

Laser Doppler flowmetry was used to evaluate changes of cerebral perfusion [5]. This instrumentation is based on the direct detection of the velocity and number of red blood cells flowing through microvessels passing through a 1mm<sup>3</sup> volume at the top of the probe [5]. It has the advantage that it provides a relatively noninvasive continuous assessment of flow. However, a disadvantage of this technique is that only relative values of flow can be obtained; therefore, once the probe is set it cannot be moved. In these experiments the probe was firmly set on the cranial window just above the brain surface. Perfusion, ICP and

## Report Documentation Page

<b>Report Date</b> 25 Oct 2001	<b>Report Type</b> N/A	<b>Dates Covered (from... to)</b> -
<b>Title and Subtitle</b> Intracranial Pressure Monitoring: Relationship Between Indices of Cerebrovascular Reserve, System Bandwidth, and Cerebral Pefusion		<b>Contract Number</b>
		<b>Grant Number</b>
		<b>Program Element Number</b>
<b>Author(s)</b>		<b>Project Number</b>
		<b>Task Number</b>
		<b>Work Unit Number</b>
<b>Performing Organization Name(s) and Address(es)</b> Department of Electrical and Computer Engineering University of Memphis Memphis, TN		<b>Performing Organization Report Number</b>
<b>Sponsoring/Monitoring Agency Name(s) and Address(es)</b> US Army Research, Development & Standardization Group (UK) PSC 803 Box 15 FPO AE 09499-1500		<b>Sponsor/Monitor's Acronym(s)</b>
		<b>Sponsor/Monitor's Report Number(s)</b>
<b>Distribution/Availability Statement</b> Approved for public release, distribution unlimited		
<b>Supplementary Notes</b> Papers from 23rd Annual International Conference of the IEEE Engineering in Medicine and Biology Society, October 25-28, 2001, held in Istanbul, Turkey. See also ADM001351 for entire conference on cd-rom.		
<b>Abstract</b>		
<b>Subject Terms</b>		
<b>Report Classification</b> unclassified		<b>Classification of this page</b> unclassified
<b>Classification of Abstract</b> unclassified		<b>Limitation of Abstract</b> UU
<b>Number of Pages</b> 3		

ABP recordings were digitized at a rate of 250 Hz with a system previously described [1,2].

A calculation of percent change of resistance were based on the following analysis. By using Poiseuille's law of flow with an approximation that is the viscosity of the fluid is constant [6], percent change of resistance can be expressed as:

$$\% \Delta R = \left( \frac{d_1^4}{d_2^4} - 1 \right) \times 100 \quad (1)$$

where d is diameter of arteriole.

Using MATLAB software (Mathworks, Inc., Natick, MA), an algorithm was developed to obtain the bandwidth of the second order transfer function between an ABP input and an ICP output that demonstrated the minimum least square error. In addition the algorithm computed corresponding values of the CorrX, mean ABP, mean ICP, and mean cerebral perfusion pressure.

### III. RESULTS

Dilatory challenge produced by ventilation with CO<sub>2</sub> generally produces a characteristic sequence of events (see Fig. 1). Initially mean ABP increases and then decreases. However, a

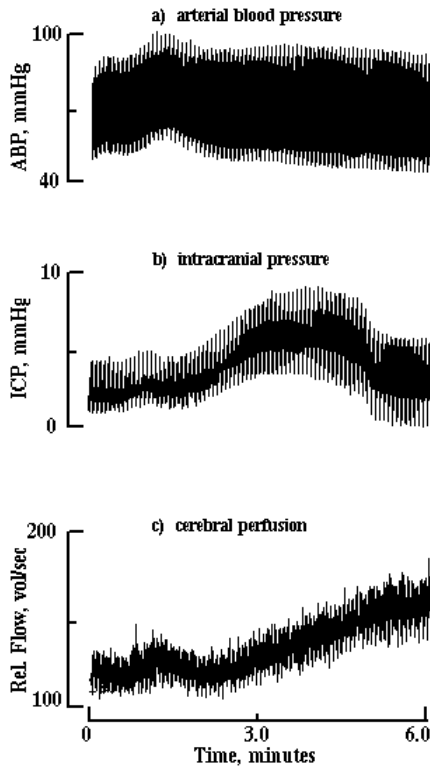


Figure 1. Changes of ABP, ICP, and Cerebral Perfusion during a Dilatory Challenge. Onset of dilatory challenge with CO<sub>2</sub> ventilation began just prior to time zero. After approximately 1 minute ABP recording began to increase and then slightly decrease with higher systolic/diastolic pulse pressure. Approximately 2 min after onset of challenge both ICP and cerebral perfusion began to increase. At about 3 min into the challenge ICP reached a peak plateau value and decreased 2 min later while cerebral perfusion continued to increase until reaching a steady state value at about 5.5 minutes.

marked increase of the arterial pulsatile blood pressure occurs. Approximately 2 min. following the onset of the challenge, arteriolar diameter, ICP and cerebral perfusion steadily increase. Furthermore like the corresponding ABP recording the pulsatility of ICP over each cardiac cycle also increases. Because of absorption of cerebrospinal fluid, upon reaching a maximum plateau value the ICP decreases back to a lower steady state mean value. In contrast both pial arteriolar diameter and cerebral perfusion steadily increase to maximum steady state value and remain relatively constant thereafter. The increase of arteriolar diameter decreased arteriolar resistance from 90% to 130%. As a result of the physiologic challenge, steady state mean values of the partial pressure of CO<sub>2</sub> in arterial pressure (pCO<sub>2</sub>) during hypercapnia were two to three times greater than normocapnic values. Steady-state percent change of cerebral perfusion pressure varied over a range of -18% to 12%. In addition, percent increase of steady state change in flow varied with from 38% to 149% respectively.

In general the linear correlation values for the group between most experimental variables were < 0.70. However, correlation values between % change of bandwidth and % change of CPP and %change of flow and % change of arteriolar diameter were 0.74 and .71 respectively. Also, an experimental relationship between bandwidth and CorrX for each experiment was determined with correlation values of ranging from 0.85 to .99 (see Fig. 2). For the group the mean correlation was both strong and significant 0.94 (p< 0.01). The exponent ranged from 1.67 to 5.37 with a mean value ( $\pm$ S.D.) of 4.10 ( $\pm$ 1.52)

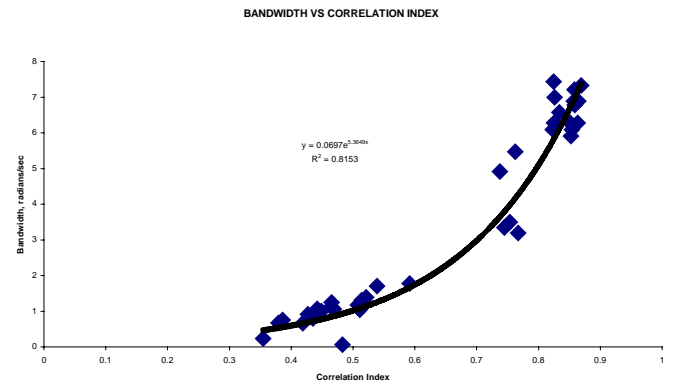


Figure 2. Example of Exponential Relationship between System Bandwidth and Correlation Index (CorrX). During normocapnia CorrX values ranged from 0.35 to 0.55 with corresponding bandwidth values below 2 radians/sec. During the dilatory challenge values of bandwidth increased exponentially with increasing CorrX values.

### IV. DISCUSSION

In this preparation, dilatory physiologic challenge by induction of hypercapnia due to ventilation with CO<sub>2</sub> generally produces a standard sequence of responses. Both mean ABP and pulsatile ABP will increase within 1.5 min of the onset of the challenge. ICP, arteriolar diameter, and cerebral perfusion generally begin to increase steadily between 2 to 3 minutes after initial challenge.

However, unlike arteriolar diameter and cerebral perfusion which reach a steady state plateau after about 5 min, ICP reaches a peak plateau and begins to decrease between 4 and 5 min. after challenge.

As expected the proposed indices of cerebrovascular reserve also increased during physiologic challenge. Previously it has been shown that changes in the CorrX index correspond to changes in arteriolar diameter [2] and when both indices approach unity the cerebral vasculature is maximally dilated [7]. With hindsight, the failure of this study to demonstrate a significant correlation between cerebral perfusion and any of the experimental variables may relate to placement of the laser probe on the cranial window rather than on brain tissue. Specifically, with such placement the 1 mm<sup>3</sup> control volume for the instrumentation was filled with a variable tissue volume. As a result, for the same absolute perfusion, the estimate of relative flow was dependent on the amount of tissue volume under interrogation. Moreover, the tissue volume also varied during the experiment because of brain movement during respiration and brain swelling during the dilatatory challenge. Placement of the probe on the brain surface would have eliminated a likely major source of error in the estimate of relative flow. Another confounding variable related to flow may have been the variability of change in CPP during challenge across experimental preparations. While not determined to be statistically significant the linear correlation value between % change of flow and % change of CPP of 0.74 indicates that variations of CPP linked to corresponding variation in cerebral perfusion.

Our finding of the exponential relationship between the bandwidth and the CorrX index of cerebrovascular reserve relates to previous studies reported by Portnoy and his colleagues. They demonstrated from laboratory studies on hypercapnic preparations that during normal tone the ABP and ICP recordings do not look similar [8,9]. In contrast, during deep hypercapnia and maximal vascular dilation, when the brain has lost the ability to autoregulate flow, these pressure recordings look very similar [8,9]. The numerical approach this earlier group used to exploit their laboratory findings was to examine changes in the coherence function derived from the ICP and ABP recordings. Specifically, over a limited frequency range, they employed spectral analysis techniques to determine the ratio of the energy in the cross-correlated ICP and ABP recordings to the product of the energy in each recording. When these pressure recordings are similar the coherence function approaches unity. Since the CorrX index derived with time domain analysis techniques is analytically equivalent to coherence analysis in the frequency domain, it is not surprising that a relationship between bandwidth of the identified model and the CorrX index exists. However, the exponential relationship may relate to the presence of a physiological mechanism. It is reasonable to assume that at adequate levels of CPP as the vasculature dilates the system becomes stiffer thus allowing higher frequencies of the driving ABP input pressure to pass. Apparently, near minimal tone, progressive loss of tone leads to changes of stiffness that produce large changes in system bandwidth.

## V. CONCLUSION

The results of this study failed to demonstrate significant relationships between changes in cerebral perfusion as measured by laser flowmetry and proposed indices of cerebrovascular reserve. However, a methodological error caused by placement of the laser flow probe above rather than on brain tissue likely introduced significant error in the estimates of relative flow prior to and during physiological dilatatory challenge. A highly significant exponential correlation between system bandwidth and CorrX, a proposed index of cerebrovascular reserve was determined. Such a relationship suggests that near minimal tone progressive loss of tone leads to changes of stiffness that produce large changes in system bandwidth.

## ACKNOWLEDGEMENTS

Funding from the National Institutes of Health awarded to M.L.D and C.W.L. supported this study.

## REFERENCES

- [1] M. L. Daley, H. Pasupathy, M. Griffith, J. T. Robertson, and C. W. Leffler, "Detection of loss of cerebral vascular tone by correlation of arterial and intracranial pressure signals," *IEEE Transactions on Biomedical Engineering*, vol. 42, pp. 420-424, 1995.
- [2] M. L. Daley and C. W. Leffler, "Correlation Coefficient between ICP and Arterial Pressure: A gauge of Cerebral Vascular Dilation," *Acta Neurochirurgica (Suppl)*, vol. 71, pp. 285-288, 1998.
- [3] M.. Czosnyka, P. Smielewski, P. Kirkpatrick, R. Laing, D. Menon, and J. D. Pickard, "Continuous assessment of the cerebral vasomotor reactivity in head injury," *Neurosurgery*, vol. 41, pp. 11-19, 1997.
- [4] J. F. Karus and D. L. McArthur, "Epidemiologic aspects of brain injury," *Neurol Clin*, vol. 4(2), pp. 435-450, 1996.
- [5] R. L. Haberl, A. Villringer, and U. Dirnagl, "Applicability of Laser-Doppler Flowmetry for Cerebral Blood Flow Monitoring in Neurological Intensive Care," *Acta Neurochir*, vol. 59, pp. 64-68, 1993.
- [6] Y. C. Fung, "Blood Flow in heart, lung, arteries and veins," In *Biomechanics: motion, flow, stream, and growth*, New York: Springer-Verlag, 1990, pp. 184-184.
- [7] M.L.Daley, M. Pourcyrous, M., A. Willis, and C. Leffler, "Variation of Proposed Correlation Indices of Cerebrovascular Reactivity with Change of Arteriolar Diameter" *Acta Neurochirurgica* Accepted, Jan, 2001.
- [8] M. Chopp and H. D. Portnoy: System analysis of intracranial pressure. *J. Neurosurgery* vol. 53, pp. 516-527, 1980.
- [9] H. D. Portnoy and M. Chopp, "Cerebrospinal fluid pulse wave form analysis during hypercapnia and hypoxia," *Neurosurgery* vol. 9, pp. 14-27, 1981.